II. REMARKS

Formal Matters

Claims 7-41 are pending after entry of the amendments set forth herein.

Claims 1-18 were examined and were rejected. Claims 19-28 were withdrawn from consideration.

Claims 1-6 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Claims 29-41 are added. Support for new claims 29-41 is found in the claims as originally filed, and throughout the specification, including the following exemplary locations: claim 29: paragraphs 0044-0065; claims 30-32: paragraph 0094; claims 33-36: paragraph 0095; claim 37: paragraphs 0096-00106; claim 38: paragraph 0079; claims 39-41: paragraph 0069. Accordingly, no new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Objection to the specification

The specification was objected to. The Office Action stated that the brief description of the drawings is deficient; and stated that Figure 5 is deficient because it fails to clearly identify which amino acid sequence corresponds to which sequence identifier.

Figure 5B is a continuation of 5A. A designation (e.g., AAL29460, P04606, P04326, etc.) appears at the beginning of each sequence, as shown in Figure 5A. The sequence identifier appears at the end of each sequence, as shown in Figure 5B. Thus, Figures 5A and 5B provide sequence identifiers corresponding to each sequence. As such, neither the brief description of the drawings nor Figures 5A/5B need be amended.

Rejection under 35 U.S.C. §102(b)

Claims 1-3 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Deng et al. ((2000) *Virology* 277:278-295; "Deng"). Claims 1-3 were rejected under 35 U.S.C. §102(a), or alternatively under 35 U.S.C. §102(b), as allegedly anticipated by by Mujtaba et al. ((2002) *Mol. Cell* 9:575-586; "Mujtaba").

Claims 1-3 are cancelled without prejudice to renewal, thereby rendering rejection of these claims moot.

Rejections under 35 U.S.C. §103(a)

Claims 4 and 5 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Deng in view of Wildey et al. ((1998) *Endocrinol.* 123:2054; "Wildey"). Claims 4 and 5 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Mujtaba in view of Wildey. Claims 6-18 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Deng in view of Wildey and Gu et al. (U.S. Patent Publication No. 2002/0001589; "Gu"). Claims 6-18 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Mujtaba in view of Wildey and Gu.

Claims 4 and 5

Claims 4 and 5 are cancelled without prejudice to renewal, thereby rendering the rejections under 35 U.S.C. §103(a) of these claims moot.

Claims 6-18 over Deng in view of Wildey and Gu

Claim 6 is cancelled without prejudice to renewal, thereby rendering this rejection of claim 6 moot.

According to MPEP § 2142, to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The Office Action has not established a *prima facie* case of obviousness. There is no motivation to combine the references. The cited references do not provide a reasonable expectation of success. In

the absence of the insight provided by the instant specification, that an acetylated Tat polypeptide is immunogenic, there would be no motivation to make an immunogenic composition comprising an acetylated Tat polypeptide, and there would have been no reasonable expectation of success. As such, Deng, alone or in combination with Wildey or Gu, cannot render any of claims 7-18 obvious.

The Office Action stated that: 1) Deng provides acetylated HIV-1 Tat (Ac-Tat) peptides, acetylated at Lys^{50}, and comprising the core sequence SYGRKKRRQ; 2) Wildey demonstrates that attaching a C-terminal cysteine residue to a polypeptide facilitates its conjugation to a carrier protein; and 3) Gu provides immunogenic compositions comprising polypeptides linked to a carrier (e.g., tetanus toxoid) through a linker containing an adjuvant (e.g., alum). The Office Action concluded that it would have been obvious to one of skill in the art to prepare immunogenic compositions, as taught by Gu, comprising the Ac-Tat polypeptides of Deng and Wildey. Applicants respectfully traverse the rejection.

Applicants note that claim 7 does not require the presence of a Cys at the carboxyl terminus of the Ac-Tat polypeptide. As such, Wildey does not appear to be relevant to claim 7. Applicants further note that Gu requires the presence in the conjugate of an immunogenic carrier. Claim 7 does not require any such carrier. As such, Gu does not appear to be relevant to claim 7.

The Office Action stated that Gu provides immunogenic compositions comprising polypeptides linked to a carrier (e.g., tetanus toxoid) through a linker containing an adjuvant (e.g., alum). However, Gu relates to a conjugate vaccine comprising lipooligosaccharide from which an esterified fatty acid has been removed (dLOS), conjugated to an immunogenic carrier. Gu, Abstract; and paragraph 0008. Gu states that the immunogenic carrier is a protein (e.g. tetanus toxoid). Gu, paragraph 0008.

Gu indicates that the dLOS by itself did not elicit antibodies to LOS, while dLOS conjugated to an immunogenic carrier such as tetanus toxoid elicited significant antibody levels. Gu, paragraph 0063 and Table 2. Gu also indicated that it was known that dLOS is poorly immunogenic. Gu, paragraph 0006. Thus, it is the immunogenic carrier that provides for the immunogenicity of the conjugate of Gu.

The present invention as claimed relates to the discovery that HIV Tat protein, which is poorly immunogenic, becomes highly immunogenic when acetylated. Specification, paragraph 0032.

Deng discusses acetylation of Tat, and states that acetylation of Tat increases transcription of integrated HIV-1 genome and enhances binding to core histones. There is no teaching or suggestion in Deng that an Ac-Tat polypeptide is immunogenic. There is no teaching or suggestion in Deng of any immunogenic composition comprising an Ac-Tat polypeptide.

Wildey does not cure the deficiency of Deng. Wildey merely discusses coupling of a synthetic heptapeptide to KLH via a C-terminal cysteine residue.

Gu does not cure the deficiency of Deng. Gu merely discusses a conjugate of a poorly immunogenic lipooligosaccharide with an immunogenic carrier, e.g., tetanus toxoid.

There is no motivation to modify the primary reference, or to combine the teachings of the cited references.

The primary reference, Deng, discusses acetylation of Tat, and states that acetylation of Tat increases transcription of integrated HIV-1 genome and enhances binding to core histones. There is no teaching or suggestion in Deng that an Ac-Tat polypeptide is immunogenic. There is no teaching or suggestion in Deng of any immunogenic composition comprising an Ac-Tat polypeptide. Wildey merely discusses coupling of a synthetic heptapeptide to KLH via a C-terminal cysteine residue. Gu merely discusses a conjugate of a poorly immunogenic lipooligosaccharide with an immunogenic carrier, e.g., tetanus toxoid.

Without the insight provided by the instant application, that an acetylated Tat polypeptide is immunogenic, there would be no reason for a person of skill in the art to make an immunogenic composition comprising an Ac-Tat polypeptide. As such, there is no motivation to combine the references.

The cited art does not provide a reasonable expectation of success.

As discussed above, Deng discusses acetylation of Tat, and states that acetylation of Tat increases transcription of integrated HIV-1 genome and enhances binding to core histones. There is no teaching or suggestion in Deng that an Ac-Tat polypeptide is immunogenic. There is no teaching or suggestion in Deng of any immunogenic composition comprising an Ac-Tat polypeptide. Wildey merely discusses coupling of a synthetic heptapeptide to KLH via a C-terminal cysteine residue. Gu merely

discusses a conjugate of a poorly immunogenic lipooligosaccharide with an immunogenic carrier, e.g., tetanus toxoid.

Without the insight provided by the instant application, that an acetylated Tat polypeptide is immunogenic, there would be no reasonable expectation of success that an immunogenic composition could be made with an Ac-Tat polypeptide. As such, the cited art does not provide a reasonable expectation of success.

Claims 6-18 over Mujtaba in view of Wildey and Gu

Claim 6 is cancelled without prejudice, thereby rendering this rejection of claim 6 moot.

The Office Action stated that: 1) Mujtaba provides acetylated HIV-1 Tat peptides, acetylated at Lys^{50}, and comprising the core sequence SYGRKKRRQR; 2) Wildey demonstrates that attaching a C-terminal cysteine residue to a polypeptide facilitates its conjugation to a carrier protein; and 3) Gu provides immunogenic compositions comprising polypeptides linked to a carrier (e.g., tetanus toxoid) through a linker containing an adjuvant (e.g., alum). The Office Action concluded that it would have been obvious to one of skill in the art to prepare immunogenic compositions, as taught by Gu, comprising the Ac-Tat polypeptides of Mujtaba and Wildey. Applicants respectfully traverse the rejection.

The Office Action has not established a *prima facie* case of obviousness. There is no motivation to combine the references. The cited references do not provide a reasonable expectation of success. In the absence of the insight provided by the instant specification, that an acetylated Tat polypeptide is immunogenic, there would be no motivation to make an immunogenic composition comprising an acetylated Tat polypeptide, and there would have been no reasonable expectation of success. As such, Mujtaba, alone or in combination with Wildey or Gu, cannot render any of claims 7-18 obvious.

As noted above, claim 7 does not require the presence of a Cys at the carboxyl terminus of the Ac-Tat polypeptide. As such, Wildey does not appear to be relevant to claim 7. Applicants further note that Gu requires the presence in the conjugate of an immunogenic carrier. Claim 7 does not require any such carrier. As such, Gu does not appear to be relevant to claim 7.

The Office Action stated that Gu provides immunogenic compositions comprising polypeptides linked to a carrier (e.g., tetanus toxoid) through a linker containing an adjuvant (e.g., alum). However, Gu relates to a conjugate vaccine comprising lipooligosaccharide from which an esterified fatty acid has been removed (dLOS), conjugated to an immunogenic carrier. Gu, Abstract; and paragraph 0008. Gu states that the immunogenic carrier is a protein (e.g. tetanus toxoid). Gu, paragraph 0008.

Gu indicates that the dLOS by itself did not elicit antibodies to LOS, while dLOS conjugated to an immunogenic carrier such as tetanus toxoid elicited significant antibody levels. Gu, paragraph 0063 and Table 2. Gu also indicated that it was known that dLOS is poorly immunogenic. Gu, paragraph 0006. Thus, it is the immunogenic carrier that provides for the immunogenicity of the conjugate of Gu.

The present invention as claimed relates to the discovery that HIV Tat protein, which is poorly immunogenic, becomes highly immunogenic when acetylated. Specification, paragraph 0032.

Mujtaba discusses the structural basis of lysine-acetylated HIV Tat recognition by the bromodomain of p300/CBP-associated factor (PCAF). Mujtaba, Summary. Mujtaba is concerned with understanding the interaction of PCAF with acetylated HIV Tat, and the effect of the interaction on HIV-1 TAR RNA binding to lysine-acetylated Tat. There is no teaching or suggestion in Mujtaba that an Ac-Tat polypeptide is immunogenic. There is no teaching or suggestion in Mujtaba of any immunogenic composition comprising an Ac-Tat polypeptide.

Wildey does not cure the deficiency of Mujtaba. Wildey merely discusses coupling of a synthetic heptapeptide to KLH via a C-terminal cysteine residue.

Gu does not cure the deficiency of Mujtaba. Gu merely discusses a conjugate of a poorly immunogenic lipooligosaccharide with an immunogenic carrier, e.g., tetanus toxoid.

There is no motivation to modify the primary reference, or to combine the teachings of the cited references.

The primary reference, Mujtaba, discusses the interaction of PCAF with acetylated HIV Tat, and the effect of the interaction on HIV-1 TAR RNA binding to lysine-acetylated Tat. There is no teaching or suggestion in Mujtaba that an Ac-Tat polypeptide is immunogenic. There is no teaching or suggestion in Mujtaba of any immunogenic composition comprising an Ac-Tat polypeptide. Wildey merely discusses coupling of a synthetic heptapeptide to KLH via a C-terminal cysteine residue. Gu merely

discusses a conjugate of a poorly immunogenic lipooligosaccharide with an immunogenic carrier, e.g., tetanus toxoid.

Without the insight provided by the instant application, that an acetylated Tat polypeptide is immunogenic, there would be no reason for a person of skill in the art to make an immunogenic composition comprising an Ac-Tat polypeptide. As such, there is no motivation to combine the references.

The cited art does not provide a reasonable expectation of success.

As discussed above, Mujtaba discusses the interaction of PCAF with acetylated HIV Tat, and the effect of the interaction on HIV-1 TAR RNA binding to lysine-acetylated Tat. There is no teaching or suggestion in Mujtaba that an Ac-Tat polypeptide is immunogenic. There is no teaching or suggestion in Mujtaba of any immunogenic composition comprising an Ac-Tat polypeptide. Wildey merely discusses coupling of a synthetic heptapeptide to KLH via a C-terminal cysteine residue. Gu merely discusses a conjugate of a poorly immunogenic lipooligosaccharide with an immunogenic carrier, e.g., tetanus toxoid.

Without the insight provided by the instant application, that an acetylated Tat polypeptide is immunogenic, there would be no reasonable expectation of success that an immunogenic composition could be made with an Ac-Tat polypeptide. As such, the cited art does not provide a reasonable expectation of success.

Conclusion as to the rejections under 35 U.S.C.§103(a)

Applicants submit that the rejections of claims 6-18 under 35 U.S.C. §103(a) have been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejections.

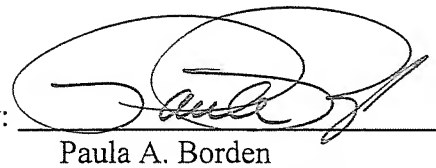
III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-296.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 27, 2007

By: 

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